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| 10/535,133 | 05/13/2005 | Anthony S Wexler | UC03-049-2 | 3588 |

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PARK, VAUGHAN & FLEMING LLP
2820 FIFTH STREET
DAVIS, CA 95618-7759

| EXAMINER | |
|---|---|
| GAKH, YELENA G | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/535,133 | WEXLER, ANTHONY S | |
| | Examiner | Art Unit | |
| | Yelena G. Gakh, Ph.D. | 1797 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☒ Claim(s) *5,15,18,25 and 28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Double Patenting*

1. Applicant is advised that should claims 12-20 be found allowable, claims 21-30 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The terms "mechanism" and "means" are synonyms in the instant context.

Examiner's Note: the examiner believes that the element "an ionizing means for ionizing the sample" is missed from claim 21.

### *Claim Objections*

2. Claims 5, 15, 18, 25, 28 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 5 does not recite any further active steps of the method. Moreover, a plurality of particles inherently consists of individual particles; also, ion mobility spectrometers are inherently designed to detect nobilities of individual particles. Claims 15 and 25 recite limitations to the particles, which are not a part of the claimed apparatus. Electrometer array is recited in the parent claims. Therefore, the claims do not further limit the structure of the apparatus from the parent claims. Claims 18 and 28 recite limitations to the sample, which is not a part of the apparatus claims, and operations on adjusting electric field and the gas flow. Optimizing parameters for the structure is not a limitation for the structure itself. Therefore, the claims do not further limit the recitation of the parent claims.

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The examiner respectfully reminds the Applicants that according to MPEP §2163, in particular, "2163.02. Standard for Determining Compliance with Written Description Requirement:

> The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co., Inc.*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting In re Kaslow, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

The Applicant failed to show "possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention". Specifically, the electrometer array recited in the claims is not disclosed as being able to analyze "the output to determine a chemical composition of the sample". The examiner failed to find any disclosure for such chemical analysis, or specific examples for electrometer arrays which are capable of chemical analysis of the output from the ion mobility spectrometer. In fact, the specification discloses that "the system analyzes the output of the electrometer array to determine the **mobility** of the analyte" (page 3, line 19). The **mobility** of the analytes *per se* does not allow determining the **chemical nature** of unknown analytes.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-4, 6-8 and 11-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 6, 13, 14, 16, 23, 24 and 26 recite the terms "desorbing" and "ablating" of the analyte; specifically "desorbing" and "ablating" "mechanism" or "means". A laser in matrix-assistant laser desorption ionization (MALDI) is used for *desorption* of the analyte from the matrix; the term "desorption" is used in the instant context in the meaning of *ablation*. Thus, the examiner does not see any difference between desorption and ablation of the analytes from the particles and considers these terms as synonyms. Laser is capable of desorbing, as well as ablating the analytes from the particles.

Claims 11 and 21 further recite "a receiving mechanism" or "a receiving means". The examiner failed to find corresponding description of these elements in the specification. The specification discloses the following: "during operation, a gas-phase sample 202 is provided to ionizer 204" (page 6, lines 6-7). Does it mean that the receiving mechanism (means) converts a liquid/solid sample into gas? The meaning of the terms is unclear.

Claim 7 recites that reading the output involved resetting the electrometer array, accumulating charge on elements and "reading the charge" (?) (determining the charge?). It is not clear, whether these steps are performed after the analytes reach the electromagnetic array, according to the parent claim. If the analytes reach the electromagnetic array, then it is not apparent, as to why the array should be reset, since the measurements will be lost at this point of time. It appears that the sequence of the steps recited in claim 7 contradicts those recited in claim 1.

Corresponding function is recited in apparatus claims 17 and 27. It is not clear from claims 17 and 27, as to whether there should be special electrometer arrays that are capable of being reset and charged? If any electrometer array is capable of being reset and charged, then claims 17 and 27 do not recite any further limitations to the parent claims 11 and 21.

Claims 8, 18 and 28 recite "a particle phase". It is not apparent, as to what phase this is. The examiner is aware of three phases for a material - solid, liquid, and gaseous. Which of these phases the "particle phase" belongs to?

Claims 11 and 21 appear to recite the structural elements through their function, as can be seen from the recitation following the clause "wherein". However, it is not apparent from the claims the way they are written, as to which structural elements of the apparatus provide this function. The functional language of the claim does not give a clear and unambiguous description of the structural elements of the apparatus, which renders the claims and all pending claims unclear and indefinite.

Claims 13 and 14 recite functional language for the apparatus claims. It is not clear, whether the functions are performed by specific structural elements of the apparatus; this renders the claims unclear and indefinite. The same is true for claims 17-20 and 27-30. The apparatus claims are supposed to recite structural elements. Therefore, if the Applicant wants to indicate e.g. that the apparatus comprises two separate electrometer arrays for detecting positive and negative ions, this should be indicated so in the claims.

Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: an ionizing means for ionizing the sample. The apparatus is not enabled without this structural element, and therefore the element is essential for proper

operation of the apparatus. Moreover, the limitation "the ionized sample" does not have an antecedent basis.

***Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

6. **Claims 1-5, 7-8, 10-15, 17-18, 20-25, 27-28 and 30** are rejected under 35 U.S.C. 102(a) as being anticipated by Fuerstenau et al. (Int. J. Mass Spectrom., April 2002) (Fuerstenau) as evidenced by any of the prior art cited in the review by Schmitt et al. (Joint Conference, March 2004) (PA Schmitt).

Fuerstenau discloses "Active pixel sensors for mass spectrometry" (Title):

"Active pixel sensors (APS) are micro-fabricated CMOS amplifier arrays that are rapidly replacing CCD devices in many electronic imaging applications. Unlike the pixels of a CCD device, the sensing elements of the APS will respond to locally situated electrostatic charge, owing to the amplifier present in each pixel. We have built two small test arrays with microscopic aluminum electrodes integrated onto standard APS readout circuitry for the purpose of detecting low-energy gas-phase ions in mass spectrometers and other analytical instruments. The devices exhibit a near-linear dynamic range greater than four orders of magnitude, and a noise level of less than 100 electrons at room temperature. Data are presented for the response of the APS detectors to small ions in a miniature magnetic sector mass spectrometer and in an atmospheric pressure jet of helium. Data for individual highly-charged electrospray droplets are presented as well. Anticipated improvements suggest that in the near future APS ion detectors will posses noise levels approaching 10 electrons and will have a useful dynamic range over six orders of magnitude." (Abstract).

Specifically Fuerstenau indicates:

"APS detectors should find use in **ion mobility instruments** as well, particularly those based on **differential ion mobility in which a spatial separation of the ions is created**. We have also been able to make this linear array detector respond to individual charged dust particles with a few thousand charges, although, the 2D array detector is better suited for this purpose." (Pages 108-109).

As evidenced by PA Schmitt:

"Differential Mobility Analysis (DMA) was originally developed to measure the mobility of charged aerosol particles. Recent extensions of the technology now permit the use of DMA to

> measure the mobility of molecular ions. [3,4,5,6,7] DMA employs a high speed flow of air contained in the annular region between two concentric cylinders (see Figure 2). *The inlet converges to accelerate the laminar air flow into the measurement cell.* Careful attention is paid to the details of the flow path to assure smoothness in order to prevent unwanted transition to turbulence. In recent tests, the DMA has operated with laminar flow at Reynolds number up to 100,000, an extraordinarily high value for non-turbulent flow. A photo of the experimental DMA flow cell at Yale University is shown in Figure 3. *High voltage (up to 19 kV) is applied between the cylinders generating* ***an electric field perpendicular to the streamlines of the high speed air flow.*** [*Claims 10, 20, 30*]. Cell polarity may be reversed to measure analyte ions of either charge. Analyte molecules may be ionized by conventional beta irradiation emitted from a radioisotope or by interaction with Electrospray Droplets that is discussed further below. Analyte ions are introduced into the DMA measurement cell on one side of the flow field. The electric field drives the ions across the streamlines while the air flow drags the ions downstream. These competing forces separate the ions in space. Ions with differing mobilities follow different trajectories across the cell: high mobility ions move directly across the air flow whereas ions with low mobility are dragged further downstream." (Page 3, the first two paragraphs of the Chapter "Differential Mobility Analysis").

Thus, Fuerstenau, as evidenced by PA Schmitt, suggests a method for performing ion mobility spectrometry, specifically a well known method of Differential Mobility Analysis (DMA), which comprises "receiving a gaseous sample for analysis, ionizing the sample, injecting the ionized sample into a laminar gas flow, wherein an electric field crosses the laminar gas flow so that the laminar gas flow and the electric field combine to spatially separate ions of the sample based on ion mobility and so that the spatially separated ions contact different elements of an electrometer array, reading an output of the electrometer array; and analyzing the output to determine a chemical composition of the sample (*Claims 1, 11, 21*), wherein a plurality of particles comprising individual particles are converted into gas phase by ablating/desorption (*Claims 2-5, 12-15, 22-25*) and are spread along the APS arrays according to their mobility upon adjusting electric field and the laminar gas flow (*Claims 8, 18, 28*).

Regarding *Claims 7, 17 and 27* Fuerstenau teaches:

> "Most imaging devices operate in a sample and hold readout mode. Charge is integrated for a precise time duration and then sampled for a time that is on the order of microseconds or less. Typically, this operation is carried out in a rolling sequential fashion, i.e., one pixel is read out while the rest are integrating the signal. Large format arrays (512 × 512) can be read out at several frames per second." (Page 102, right column). Ground calibration of APS detectors is inherent to a detection mode.

### *Claim Rejections - 35 USC § 103*

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. **Claims 6, 16 and 26** are rejected under 35 U.S.C. 103(a) as being unpatentable over Fuerstenau as evidenced by PA Schmitt in view of Koomen et al. (Anal. Bioanl. Chem., June 2002) (Koomen).

Fuerstenau as evidenced by PA Schmitt does not specifically disclose tandem ion mobility spectrometry/spectrometer for detecting analytes obtained by ablation and desorption.

Koomen teaches "Oligonucleotide analysis with MALDI–ion-mobility–TOFMS" (Title), which comprises using laser desorption from matrix for obtaining desorbed/ablated analytes to be introduced into the ion mobility spectrometer.

It would have been obvious for a person of ordinary skill in the art to use tandem ion mobility spectrometer using laser desorption/ablation technique as taught by Koomen in order to obtain the most complete analysis of the compounds, which may be not fully released into the first ion mobility spectrometer.

10. **Claims 8, 18 and 28** are rejected under 35 U.S.C. 103(a) as being unpatentable over Fuerstenau as evidenced by PA Schmitt.

While Fuerstenau as evidenced by PA Schmitt does not specifically disclose separate electrometer array for positive and negative ions, it would have been a clear modification of Fuerstenau's method and apparatus, since Schmitt indicates that "[c]ell polarity may be reversed to measure analyte ions of either charge" (page 3). Thus, it would have been obvious for a

person of ordinary skill in the art to measure both types of ions sequentially at two different sets of electrometer APS arrays.

***Conclusion***

11. The art made of record and not relied upon is considered pertinent to applicant's disclosure. *Zhang and Wexler (Int. J. Mass Spectrom., 2006)* teach "Cross flow ion mobility spectrometry: Theory and initial prototype testing".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

12/4/2008

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797